

In re Application of Shen et al.,
S.N. 10/768,825
Filed: 02/27/2004
Attorney Docket No. LA0100

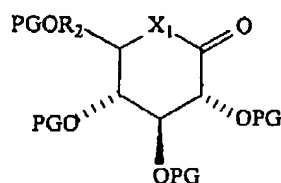
AMENDED CLAIMS

What is claimed:

1. (Currently Amended) A method of making glycosides using a non-cryogenic process comprising, in a continuous process, the steps of:
 - (a) lithiating an aromatic reactant having a leaving group using a lithium reagent in a first microreactor ~~under~~ at non-cryogenic ~~conditions~~ temperatures to form a lithiated anion species; and
 - (b) coupling the lithiated anion species with a carbonyl substituted reactant to form a glycoside.
2. (Original) The method according to claim 1, wherein said lithiating step is performed at a temperature of from about -10°C to about 20°C.
3. (Original) The method according to claim 2, wherein said lithiating step is performed at a temperature of from about -10°C to about 5°C.
4. (Original) The method according to claim 1, wherein the residence time in said first microreactor is from about 2 seconds to about 3 seconds.
5. (Original) The method according to claim 1, wherein said aromatic reactant is a halide.
6. (Original) The method according to claim 1, where said lithium reagent is selected from the group consisting of n-BuLi and t-BuLi.
7. (Original) The method according to claim 1, wherein a yield of said glycoside is greater than about 80%.
8. (Currently Amended) The method according to claim 1, wherein said coupling step is performed ~~under~~ at cryogenic ~~conditions~~ temperatures.
9. (Original) The method according to claim 8, wherein said coupling step is performed at a temperature of less than about -80°C.
10. (Original) The method according to claim 1, wherein said coupling step is performed in a second microreactor under non-cryogenic conditions.

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11. (Original) The method according to claim 10, wherein said coupling step is performed at a temperature of from about -20°C to about 20°C.
12. (Original) The method according to claim 11, wherein said coupling step is performed at a temperature of about -10°C.
13. (Original) The method according to claim 10, wherein the residence time in said second microreactor is from about 2 seconds to about 3 seconds.
14. (Original) The method according to claim 10, wherein a yield of said glycoside is greater than about 70%.
15. (Currently Amended) A method of making glycosides using a non-cryogenic process comprising, in a continuous process, the steps of:
 - (a) lithiating an aromatic reactant having a leaving group using a lithium reagent to form a lithiated anion species; and
 - (b) coupling the lithiated anion species with a carbonyl substituted reactant according to formula IV



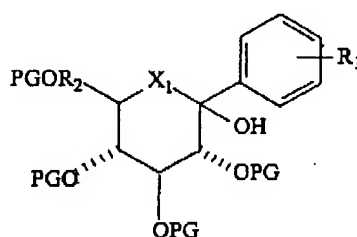
[IV]

in a microreactor under non-cryogenic conditions to form a glycoside.

16. (Original) The method according to claim 15, wherein said coupling step is performed at a temperature of from about -10°C to about 20°C.
17. (Original) The method according to claim 15, wherein said coupling step is performed at a temperature of from about -10°C to about 5°C.
18. (Original) The method according to claim 15, wherein the residence time in said microreactor is from about 2 seconds to about 3 seconds.

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19. (Currently Amended) The method according to claim 15, wherein said lithiating step is performed ~~under~~ at cryogenic conditions temperatures.
20. (Original) The method according to claim 1, further comprising the step of :
(c) deprotecting the glycoside.
21. (Original) A glycoside formed by the method of claim 1.
22. (Currently Amended) A ~~method of~~ continuous process for making a glycoside having the general structural formula [I]:

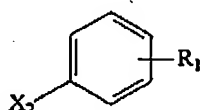


[I]

wherein: R₁ is hydrogen, NO₂, OR₄, a halogen, or a substituted or non-substituted alkyl, aryl, or heterocycle; R₂ is a substituted or non-substituted alkyl group; ~~wherein~~ R₄ is a substituted or non-substituted alkyl or aryl; X₁ is a heteroatom; and PG is a protective group,

the method including the steps of:

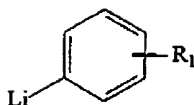
- (a) reacting an aromatic reactant having general structural formula [II]:



[II]

wherein: R₁ is as defined previously and X₂ is a leaving group, in a first microreactor with an organo lithium reagent to form a lithiated anion species having general structural formula [III]:

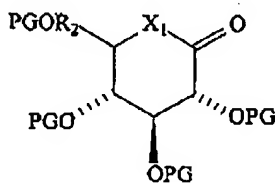
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[III]

wherein R₁ is as defined previously, and

(b) coupling the lithiated anion species [III] with a carbonyl substituted compound having general structural formula [IV]:



[IV]

wherein: R₂, X₁ and PG are as described previously, to form the compound having general structural formula [I].

23. (Original) The method of claim 22 wherein the lithiating step is performed at a temperature of from about -10°C to 20°C.
24. (Currently Amended) The method of claim 23 wherein the coupling step is performed in a second microreactor under at non-cryogenic conditions temperatures.
25. (Original) The method of claim 23 wherein the lithiating step is conducted in a solvent selected from THF/toluene or THF/heptane.
26. (Currently Amended) The method of claim 23 wherein the coupling step is performed in a second microreactor under at non-cryogenic conditions temperatures.
27. (Original) The method of claim 26 wherein the coupling step is performed at a temperature of from about -20°C to 20°C.